

EXHIBIT B17

two latent change-point states within VENG: one of high change-point frequency, and one of low change-point frequency indicated an underlying structure in fetal and neonatal VENG.

CONCLUSION: HRV monitoring tracks fetal and neonatal inflammatory response using abdominal ECG or regular precordial ECG, respectively. VNS reduces the magnitude of the neonatal inflammatory response. The proposed VENG analysis can provide insights into dynamics of vagal signalling to optimize the anti-inflammatory VNS regimens. This is clinically relevant because VNS can be done non-invasively.

*Figure(s) will be available online.

F-096

Use of Songs to Improve Knowledge of Antenatal Care in a Predominantly Illiterate Community. Binod B. Sharma,¹ Deborah Loxton,² Henry Murray,³ Giavanna Angeli,² Simon Chiu,² Christopher Oldmeadow,¹ Roger Smith.¹ ¹Hunter Medical Research Institute (HMRI), New Lambton, Australia; ²Hunter Medical Research Institute HMRI, New Lambton, Australia; ³John Hunter Hospital, New Lambton, Australia; ⁴University of Newcastle, Newcastle, Australia; ⁵University of Newcastle Australia, New Lambton, Australia.

INTRODUCTION: In many rural villages of Nepal, the maternal mortality rate is amongst the highest in the world. The reasons for this are cultural, illiteracy and lack of knowledge about the needs of women during pregnancy. The death of a woman in childbirth is just accepted. Culturally, singing and dancing are part of Nepalese daily life in rural settings. We hypothesized that health messages regarding the importance of antenatal care might be effectively transmitted by songs in the limited literacy environment of rural Nepal.

METHODS: We randomly grouped four rural Village Development Committees comprising 36 villages into two (intervention and control) clusters. In the intervention group, community members were provided with key health messages regarding pregnancy and childbirth, and different local groups were invited to write song lyrics incorporating the messages to accompany locally popular melodies. The local groups presented their songs and dance in a community festival organised and judged by the community. The winning songs were performed by the local people in a song and dance procession through the villages, houses and fields. A wall chart with key health messages was also provided to each household. Knowledge of household decision makers (senior men and women) was assessed before and after the intervention using a structured questionnaire in all households. Each stage of the process was video recorded.

RESULTS: Baseline and post-intervention survey (intervention n=735, control n=775) data was collected. Knowledge scores were evaluated as the number of correct items out of 36 questions. Knowledge improved significantly in the intervention group, improving from a mean of 11.60/36 to 22.33/36, an increase of 10.69 [9.97, 11.41, P<0.001]. The control population improved from 17.48/36 to 18.26/36 a mean increase of 0.81 units [0.28, 1.33]. Improvement was greatest amongst the most illiterate members of the community [6.8, 19.8, P<0.001]. No changes were observed in the control villages.

CONCLUSION: The use of singing bypassed the limitations of literacy in communicating health messages that are key to improving maternal mortality in this rural setting within a developing country. With appropriate sociocultural adaptation to local context, this model of community education may be applicable to improve maternal health outcomes in other low resource communities.

F-097

Stromal Cell Expression of the Receptor Tyrosine Kinase DDR2 Promotes Ovarian Cancer Metastasis. Katherine Fuh,¹ Molly Greenwade,¹ Whitney Grither,¹ Hollie Beck,¹ Daniel Wilke,¹ Ian Hagemann,¹ Andrea Hagemann,¹ Carolyn McCourt,¹ Premal Thaker,¹ Matt Powell,¹ Dave Mutch,¹ Greg Longmore.¹ ¹Washington University, St. Louis, MO, United States.

INTRODUCTION: Understand the role of stromal discoid domain receptor 2 (DDR2) expression in ovarian cancer metastasis.

METHODS: Immunohistochemistry was performed of short-term (<3 years) versus long-term (>5 years) high-grade serous ovarian cancer tumors through the Washington University Gynecologic Oncology Tissue bank. Stromal and tumor cell expression of DDR2 was scored for intensity and frequency. To determine the effect of metastasis with DDR2 deficient stromal cells, global DDR2 knockout (KO) mice (DDR2 deficient) were compared to DDR2 wild-type (WT) mice (DDR2 expressing) when a DDR2 expressing murine tumor cell line (ID8Ttp33/-BRCA2/-) was injected intraperitoneally. Intraperitoneal spread was quantified using bioluminescence imaging (BLI) and tumor weight. Additionally, cell based mesothelial cell clearance assays utilizing human omentum-cultured mesothelial cells expressing DDR2 were compared to mesothelial cells not expressing DDR2.

RESULTS: Patients who lived <3 years had significantly higher DDR2 expression in the stroma when compared to patients living >5 years (mean DDR2 IHC score 76% vs 48%, p<0.0001). Similar findings were observed for DDR2 expression in the tumor cells, with mean IHC score 80% vs 64%, p<0.0001 in patients who lived <3 years vs >5 years. In determining the stromal effect of DDR2 in metastasis, DDR2 KO mice (DDR2 deficient in stromal cells) had less intraperitoneal spread of ovarian cancer cells than DDR2 WT by BLI (mean 5.8×10^4 vs 2.2×10^4 total photon flux, p=0.01) and by number of tumor implants (mean 6 vs 2 nodules, p=0.006). Additionally, human ovarian cancer cells plated above mesothelial cells that were DDR2 deficient had less tumor cell clearance than those tumor cells plated above mesothelial cells that expressed DDR2 (p=0.01).

CONCLUSION: The stromal contribution of DDR2 promotes tumor cell clearance of mesothelial cells and metastatic spread. This suggests that stromal expression of DDR2 may be a potential target to guide future therapy particularly in the maintenance setting.

F-098

Talcum Powder Enhances Oxidative Stress in Ovarian Cancer Cells. Nicole M Fletcher,¹ Ira Memaj,¹ Ghassan M Saed*,¹ Wayne State University, Detroit, MI, United States.

INTRODUCTION: We have previously characterized epithelial ovarian cancer (EOC) cells to manifest a persistent pro-oxidant state as evident by the upregulation of certain key oxidant and downregulation of key antioxidant enzymes. This redox state is further enhanced in chemoresistant EOC cells. Several studies have suggested possible association between genital use of talcum powder and risk of EOC; however, the biologic basis for this association has yet to be delineated. The objective of this study was to determine the effects of talcum powder on the expression of key oxidant and antioxidant enzymes in EOC cells.

METHODS: Human EOC cell lines (SKOV-3, MDAH-2774, A2780, and OV90) were obtained from ATCC and Sigma Aldrich. Human primary normal ovarian epithelial cells were obtained from Cell Biologics. Cells were treated with 0, 200, 500 µg/ml of talc (Sigma Aldrich) for 24, 48, and 72 hrs. RNA was extracted, followed by cDNA synthesis and real-time RT-PCR was performed to determine mRNA levels of key redox enzymes including myeloperoxidase (MPO), inducible nitric oxide synthase (iNOS), superoxide dismutase (SOD), catalase (CAT), glutathione S-transferase (GST), glutathione peroxidase (GPX), and glutathione reductase (GSR). Data was analyzed with oneway ANOVA. Significant comparisons were further analyzed with Tukey's post hoc tests with Bonferroni correction.

RESULTS: There was a marked increase in mRNA levels of the pro-oxidant enzymes, iNOS and MPO in talc treated ovarian cancer cell lines and normal ovarian epithelial cells, all as compared to their control, as early as 24 hours in all doses. Additionally, there was a marked decrease in the mRNA levels of the antioxidant enzymes CAT, GPX, SOD3, but with a marked increase in GSR, and no change in GST, in talc treated ovarian cancer cell lines and normal ovarian epithelial cells, all as compared to their control, as early as 24 hours in all doses.

CONCLUSION: This is the first report to show that talcum powder induces a biological effect by further enhancing the redox state in both normal ovarian epithelial cells as well as in ovarian cancer cells. The



results of this study will provide a molecular basis to previous reports that link genital use of talcum powder to increased risk of epithelial ovarian cancer.

F-099

ERAP2(N) Induced Rapid Choriocarcinoma Clearance *In Vivo*. Eun D Lee*,¹ Michelle Warhan,² Sonya Washington,³ Ronald Ramus,⁴ Efstratios Stratikos,¹ Jerome Strauss.¹ ¹National Center for Scientific Research, Demokritos, Greece; ²University of Virginia, Charlottesville, VA, United States; ³Virginia Commonwealth University, Richmond, VA, United States.

INTRODUCTION: High as 50 percent of hydatidiform mole results in life threatening gestational choriocarcinoma when the tumor metastasizes. Half of the choriocarcinoma cell lines lack endoplasmic reticulum aminopeptidase 2 (ERAP2) and have a unique HLA repertoire to study the immune mechanism. ERAP2 enzyme trims amino acid residues prior to presentation on HLA class I molecules. When the major T allele of ERAP2 changes Lysine (K) to asparagine (N) near the catalytic center of the enzyme it results in increased peptide trimming by up to 165-fold. This alters the peptide and HLA repertoire affecting the immune response. Interestingly, ERAP2(N) is not biologically detected in any population studied. Therefore, we hypothesize that ERAP2(N) can induce fatal immune response. Using an ERAP2(N) expressing choriocarcinoma cell model, our preliminary data shows that ERAP2(N) expressing cells are preferentially killed by activated NK cells *in vitro*. This observation suggests that ERAP2(N) expression in cells is immunologically unfavorable for survival.

METHODS: To further test the role of ERAP2(N) *in vivo*, we used NSG mice model system to determine its contribution to the emergence and clearance of solid tumors by adoptive transfer of immune cells compared to the tumor that does not express ERAP2(N).

RESULTS: After the lymphocyte treatment, only ERAP2(N) tumor displayed a rapid and significant decrease in tumor volume ($P=0.046$). The DiR fluorescently labeled lymphocytes were specifically targeting the tumor. The TdT Immunohistochemistry analysis of the tumor confirmed the apoptotic death by the activated lymphocyte. Lastly, the activated lymphocytes were elevated against ERAP2(N) expressing choriocarcinoma cells.

CONCLUSION: Together, the data strongly suggest that ERAP2(N) can be utilized as a potential cancer target molecule to specifically eliminate tumor.

F-100

Trends amongst Residency Programs Offering Trials of Labor after Cesarean Delivery (TOLAC). Monica Basinger*, Jerasimos Ballas*, Christina Davidson* Baylor College of Medicine, Houston, TX, United States.

INTRODUCTION: The National Institutes of Health recognizes that a trial of labor after cesarean delivery (TOLAC) is a reasonable option for many women with a prior cesarean delivery and called on organizations to facilitate access to this birth option. However, the practice of offering TOLAC varies widely throughout the United States. The purpose of our study is to determine what trends exist in the attitudes and practices of offering TOLAC between different levels of residents and Program Directors, different types of U.S. OB/GYN Residency training programs, and different regions of the country.

METHODS: A voluntary survey was sent electronically via publicly acquired e-mail addresses of Program Directors to each current U.S. OB/GYN ACGME accredited program with request to complete survey and distribute amongst their residents.

RESULTS: We had 30% (80/249) response rate from program directors and estimated 4.8% (243/5020) total resident responses, assuming every resident was distributed the survey. The majority of responses were from the Mid-Atlantic (20%) and South Atlantic (16-19%) regions. Program types were divided into four categories with the majority of responses from University based programs (60%) and Community hospital, university-affiliated (27%) followed by community based (12%) and military (1%). Both program directors and residents answered similarly in that 100% of both groups reported their program offered TOLAC to patients

with one prior cesarean, 81% offer TOLAC with two prior cesareans and 10% offer TOLAC in patients with three prior cesareans. Using chi-squared analysis, there was no statistically significant difference in offering TOLAC to different candidates in both the type of hospital and the region of the country.

In general, both groups felt the attitude of hospital nursing staff towards TOLAC was positive. The vast majority of program directors felt comfortable with their residents managing and counseling patients regarding TOLAC (99%). Likewise, most residents responded affirmatively that they are comfortable with the intrapartum management of a woman undergoing TOLAC (95%) and 82% agree that post-residency, they will offer TOLAC to appropriate candidates regardless of indication for cesarean.

CONCLUSION: Program directors and residents responded similarly in the rates of offering TOLAC to certain patients depending on risk factors. Both groups also felt confident in the ability of residents to manage these patients in labor. There were no significant differences in programs who offered TOLAC based on type of program or region of the country. Specifically, the Mid-Atlantic region (NY, NJ, and PA) was not associated with a decrease in the number of patients being offered TOLAC compared to all other regions despite these states being reported as three of the top five highest for medical malpractice payouts per capita in 2016.

F-101

Assessment of Fetal Head Position and Primary Cesarean Delivery Rate. Chelsea DeBolt*,¹ Maya Craffey*,¹ David O'Sullivan*,² Jessica Mullins*,¹ Adam Borgida*,¹ ¹Hartford Hospital, Hartford, CT, United States; ²University of Connecticut, Farmington, CT, United States.

INTRODUCTION: Occiput posterior (OP) fetal head position is associated with higher rates of cesarean delivery (CD), prolonged second stage of labor, operative vaginal delivery (OVD) and third- and fourth-degree perineal lacerations. Despite national concern for higher than recommended CD rate, few interventions have been shown to decrease the CD rate overall. The objective of this study is to evaluate if assessment of the fetal head position beyond 6 cm dilation but prior to the start of the second stage of labor is associated with a decrease in primary CD rate.

METHODS: This retrospective cohort study included nulliparous, term, singleton, vertex pregnancies delivered at Hartford Hospital from August 2016 to April 2017. The exposure group consists of patients who had assessment of fetal head position, while the control group consists of patients who did not. The primary outcome was CD rate. Groups were compared with respect to each maternal and neonatal variable and differences between groups were evaluated with a Pearson chi square test. A multivariate regression model was performed to evaluate the influence of several variables on the outcome. All data was analyzed using an a priori alpha level of 0.05.

RESULTS: 690 women met inclusion criteria for investigation, 379 women in the control group and 311 women in the exposure group. The primary CD rate was 15.9% in the control group and 22.9% in the exposure group, and this difference was not statistically significant ($p=0.078$, Table 1). Arrest of the second stage of labor was more likely to be the reason for CD in the exposure group (53.4% vs. 19.2%, $p<0.001$, Table 1), and within the second stage arrest group, persistent OP occurred in 58.1% of deliveries. The OVD rate was also higher in the exposure group (10.0% vs. 5.8%, $p=0.041$, Table 1). For those who underwent an intervention (i.e. manual rotation, position changes) within the exposure group, the rate of CD was significantly higher (42.5% vs. 22.1%, $p<0.001$).